8EHQ-0295-13329

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8EHQ-95-13329

(A) 88950000118

February 6, 1995

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
P 253 155 586

OPPT Document Processing Center (7407)
ATTN: Section 8(e) Coordinator
Office of Pollution Prevention and Toxics (OPPT)
US Environmental Protection Agency
Washington, DC 20460

RE: TSCA Section 8(e) Notice

COMPANY SANITIZED

95 FEB 13 PM 3:04

RECEIVED

Dear Sir or Madam:

This notice is being submitted by Rhône-Poulenc Ag Company (RPAC) to the Environmental Protection Agency (EPA) in accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), 15 USC § 2607 (e).

We are submitting results on a variety of compounds from the same chemical family that are being screened for research and development purposes. Only limited quantities of these compounds have been synthesized.

RPAC claims the alpha-numeric designations and the specific chemical identities of the substances at issue to be confidential business information (CBI). The chemical substances may be nonconfidentially identified as a "heterocycles".

Groups of five male mice were administered a test substance suspended in corn oil as follows:

10 mg/kg/day on Days 1 to 4
20 mg/kg/day on Days 5 to 8
40 mg/kg/day on Days 9 to 12

Surviving animals were sacrificed three days after the last dose administered on Day 12. Information on the following compounds is being submitted based on the observation of clinical signs on several occasions in several animals. Most animals died within a few days of exhibiting clinical signs. However, in a few instances, animals displaying clinical signs survived until study termination.

All mice died. Increased motor activity, excessive jumps, and irritability to touch were observed in 4 of 5 mice. These signs occurred within approximately 24 hours of death in 3 of the animals and within 48 hours of death in one animal that also exhibited convulsions within 24 hours of death.

RECEIVED 3/1/95

One of five mice died during the study. The mouse that died exhibited prostration and dyspnea on the day of death. No other clinical signs were noted during the study. Absolute liver weight at study termination was 140% above control.

All mice died. Clinical signs were noted for four mice and included increased motor activity within 48 hours of death and irritability to touch and excessive jumps within 24 hours of death in one mouse, increased motor activity in three other mice within approximately 24 hours of death, and convulsions in one mouse on the day of death.

Three of five mice died. Increased motor activity, excessive jumps, prostration, and irritability to touch were observed the two mice that survived to study termination. One of these mice also exhibited convulsions on the day prior to study termination.

All mice survived to study termination and no clinical signs were observed. Absolute liver weight at study termination was 129% above control.

All mice died. Increased motor activity was observed within 24 to 48 hours of death in four mice. Two of these mice also exhibited excessive jumps within 24 hours of death, and a third mouse exhibited prostration, hunched posture, piloerection, and irritability to touch within 24 hours of death.

Two of five mice died. The mouse found dead on Day 7 exhibited reduced motor activity on Day 7. The other mouse was found dead on Day 8 but did not exhibited any clinical signs. One mouse surviving to study termination exhibited tremors, hunched posture, staggering step, reduced motor activity, and piloerection on Day 14, the day prior to study termination. Absolute liver weight for mice surviving to study termination was 158% above control.

One of five mice died. This mouse was sacrificed moribund on Day 14 and exhibited increased motor activity and excessive jumps on Day 12, piloerection on Days 12 through 14, irritability to touch, prostration, and palpebral ptosis on Days 13 and 14, and hunched posture on Day 13. The four surviving mice exhibited increased motor activity on Days 12 and 13.

All mice died. One mouse exhibited reduced motor activity on Days 10 through 12, irritability to touch on Days 10 and 11, hunched posture on Day 11, prostration and tremors on Day 12, and loss of righting reflex on Day 13 and was found dead on Day 13. Another mouse exhibited reduced motor activity, hunched posture, and tremors on Days 11 and 12 and was found dead on Day 13.

Two of five mice died. One mouse that was found dead on Day 12 exhibited piloerection on Day 4 only. Another mouse that survived to study termination

exhibited piloerection on Day 4 and soiled fur on Day 9. Absolute liver weight for animals surviving to study termination was 104% above control.

Two of five mice died. Two mice surviving to study termination exhibited increased motor activity, hunched posture, and reduced motor activity on several days.

Two of five mice died. No clinical signs of toxicity were observed during the study. For mice surviving to study termination, absolute liver weights were 105% above control.

SUPPORT INFORMATION OF CONFIDENTIALITY CLAIMS

1. Claims of confidentiality are being made on behalf of RPAC.

2. RPAC asserts this claim of confidentiality until such time as a specific chemical is approved for use in the United States. In the event that the chemicals are never approved, RPAC asserts that the CBI information should be provided permanent protection. The structures and use of the chemicals are unique. Disclosure of this information would provide our competitors with information on facets of our business that would be detrimental to our competitive position.

3. The information claimed as confidential has not been previously disclosed to any other governmental agency or to EPA.

4. This information has been disclosed to only a very limited number of investigators outside of RPAC who have performed either toxicity or efficacy testing. These individuals operate under a strict secrecy agreement. Any individuals who may work with the chemicals will have all health/toxicology information disclosed to them as well, but only on the basis of strict secrecy and respect for the CBI nature of the information.

5. Any individuals to whom the CBI is revealed are warned of the nature of the information. Further, they are informed of their obligations to maintain secrecy should they terminate their employment with RPAC.

6. None of the information claimed as confidential appears in or is referred to in any advertising or promotional materials for the chemical or the end product containing it, professional or trade publications, or any other media available to the public or to our competitors. Appropriate warnings do appear on safety data sheets, as RPAC considers that individuals who are requested to work with the chemicals have every right to know as much about the chemicals' toxicity as possible. Further, the information is only considered to be CBI with respect to the general public, insofar as our competitors could use the information in an unfairly competitive nature.

7. No previous confidentiality determinations have been made by EPA, other Federal agencies or courts in connection with this information.

8. RPAC believes that disclosure of this information to the general public would be likely to result in substantial harm to its competitive position. Disclosure of the alpha numeric designations and chemical names would provide some competitors with information about the specific chemistry of this area of our research and our business. Further, the type of toxicological testing being reported in the TSCA 8(e) notice would provide competitive

information about this chemical's status in the research and development process and, therefore, the time remaining until commercialization.

9. A patent has not been issued for the specific chemical structures. However, the generic chemical structures are covered by a patent that is currently pending.

10. The chemicals are not available commercially. They are in the earliest stages of research and development for pesticide use and are unlikely to be developed into commercial products.

11. We believe that disclosure of the chemical names would allow a competitor to synthesize these chemicals. RPAC has invested a large amount of time and money into research of this particular chemical family, and information on specific chemical structures would harm our competitive position.

12. Disclosure of the chemical structures might reveal information on processes used to synthesize these compounds.

13. CAS numbers for these chemicals have not yet been assigned.

14. Currently, the chemicals are not the subject of FIFRA regulation or reporting.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,

Glenn S. Simon, PhD, DABT
Director of Toxicology

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Glenn S. Simon, Ph.D., DABT
Director of Toxicology
Rhône-Poulenc
P.O. Box 12014
2 T.W. Alexander Drive
Research Triangle Park, North Carolina 27709

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 18 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

13329A

Triage of 8(e) Submissions

Date sent to triage: APR 19 1995

NON-CAP CAP

Submission number: 13329A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1-4 **pages** 1-4

Notes:

Contractor reviewer : PRR **Date:** 4/3/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0295 -13329 (5) SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Ag Company

SUB. DATE: 02/06/95 OTS DATE: 02/13/95 CSRAD DATE: 03/01/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME: Heterocycles — S# Confident

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
(0213)	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
(0224)	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY
YES
CAS SR
NO
(IN ABEYANCE)
COMMENTS: Non-CAP

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES: mus

TOXICOLOGICAL CONCERN:
LOW
MED
(HIGH)

USE: R & D pesticide

PRODUCTION:

8(E)-13329A

H

SUBACUTE ORAL TOXICITY IN MALE MICE IS OF HIGH CONCERN BASED ON LETHALITY. DOSAGES (DIET, 12 DAYS, 5/GROUP) WAS 10 MG/KG/DAY (DAYS 1-4); 20 MG/KG/DAY (DAYS 5-8); AND 40 MG/KG/DAY (DAYS 9-12). RESULTS WERE REPORTED FOR 12 TEST SUBSTANCES BUT THEIR IDENTITIES WERE SANITIZED. EXCEPT FOR ONE SUBSTANCE (0/5 DEATHS), INCIDENCE OF DEATH RANGED FROM 1/5 TO 5/5. MOST ANIMALS DIED WITHIN A FEW DAYS OF EXHIBITING CLINICAL SIGNS OF TOXICITY, WHICH INCLUDED INCREASED OR REDUCED MOTOR ACTIVITY, EXCESSIVE JUMPS, IRRITABILITY TO TOUCH, TREMORS, STAGGERING STEP, PALPEBRAL PTOSIS, PROSTRATION, DYSPNEA, CONVULSIONS, HUNCHED POSTURE, AND PILOERECTION. INCREASES IN ABSOLUTE LIVER WEIGHT IN ANIMALS THAT SURVIVED TO TERMINATION WERE REPORTED FOR 5 OF THE 12 TEST ANIMALS.